510(k) Substantial Equivalence Determination
Decision Summary

MAY - 1 2012

A. 510(k) number: K121044

B. Purpose for Submission:

To determine substantial equivalence for the ***illumigene***® Group B *Streptococcus* (GBS) DNA Amplification Assay used for the qualitative detection of *Streptococcus agalactiae*.

C. Measurand:

Segment of the *Streptococcus agalactiae* genome

D. Type of Test:

Qualitative in vitro diagnostic using Loop-mediated isothermal DNA amplification (LAMP) technology

E. Applicant:

Meridian Bioscience, Inc.

F. Propriety and Established Names:

illumigene® Group B *Streptococcus* (GBS) DNA Amplification Assay

G. Regulatory Information:

Product Code	Classification	Regulation Section	Panel
NJR, Nucleic acid amplification assay system, *Streptococcus spp.*, serological reagents	Class I	21 CFR § 866.3740	Microbiology (83)

H. Intended Use:

1. Intended use(s):

The ***illumigene*** Group B *Streptococcus* (GBS) assay, performed on the ***illumipro-10***, is a qualitative *in vitro* diagnostic for the detection of *Streptococcus agalactiae* in enriched cultures obtained from vaginal/rectal swab specimens from antepartum women. Enriched cultures are obtained by 18-24 hour incubation of vaginal/rectal swab specimens in selective broth medium, Lim Broth, TransVag Broth or Carrot Broth.

The ***illumigene*** GBS assay utilizes loop-mediated isothermal DNA amplification (LAMP) technology to detect *Streptococcus agalactiae* by targeting a segment of the *Streptococcus agalactiae* genome. Results from the ***illumigene*** GBS assay can be used as an aid in establishing the GBS colonization status of antepartum women. This assay does not diagnose or monitor treatment for GBS infections. The ***illumigene*** GBS assay does not provide susceptibility results. Culture isolates are needed for performing susceptibility testing as recommended for penicillin-allergic women.

illumigene Group B *Streptococcus* is intended for use in hospital, reference or state laboratory settings. The device is not intended for point-of-care use.

2. Indication(s) for use:

The ***illumigene*** Group B *Streptococcus* (GBS) assay, performed on the ***illumipro-10***, is a qualitative *in vitro* diagnostic for the detection of *Streptococcus agalactiae* in enriched cultures obtained from vaginal/rectal swab specimens from antepartum women. Enriched cultures are obtained by 18-24 hour incubation of vaginal/rectal swab specimens in selective broth medium, Lim Broth, TransVag Broth or Carrot Broth.

The ***illumigene*** GBS assay utilizes loop-mediated isothermal DNA amplification (LAMP) technology to detect *Streptococcus agalactiae* by targeting a segment of the *Streptococcus agalactiae* genome. Results from the ***illumigene*** GBS assay can be used as an aid in establishing the GBS colonization status of antepartum women. This assay does not diagnose or monitor treatment for GBS infections. The ***illumigene*** GBS assay does not provide susceptibility results. Culture isolates are needed for performing susceptibility testing as recommended for penicillin-allergic women.

illumigene Group B *Streptococcus* is intended for use in hospital, reference or state laboratory settings. The device is not intended for point-of-care use.

3. Special Conditions for use statement(s):

- For Prescription Use Only
- The device is not intended for point-of-care use

4. Special instrument requirements:

illumipro-10™ Automated Isothermal Amplification and Detection System

I. Device Description:

The ***illumigene*** Molecular Diagnostic Test System is comprised of the ***illumigene***® Group B *Streptococcus* (GBS) DNA Amplification Test Kit, the ***illumigene*** Group B *Streptococcus* (GBS) External Control Kit and the ***illumipro-10***™ Automated Isothermal Amplification and Detection System.

The ***illumigene*** Group B *Streptococcus* (GBS) DNA amplification assay utilizes loop-mediated isothermal amplification (LAMP) technology to detect the presence of *Streptococcus agalactiae* in enriched cultures obtained from vaginal/rectal swab specimens taken from antepartum women. Each ***illumigene*** GBS assay is completed using ***illumigene*** Control Reagent, ***illumigene*** Reaction Buffer, an ***illumigene*** GBS Test Device and an ***illumigene*** Heat Treatment Tube. Samples are diluted with the ***illumigene*** Control Reagent, target DNA is made available for isothermal amplification via heat-treatment in the ***illumigene*** Heat Treatment Tube and DNA amplification occurs in the ***illumigene*** GBS Test Device.

The ***illumipro-10*** heats each ***illumigene*** GBS Test Device containing prepared samples and Control Reagent, facilitating amplification of target DNA. When *S. agalactiae* is present in the enriched culture sample, a conserved sequence of the *S. agalactiae* is amplified and magnesium pyrophosphate is formed. Magnesium pyrophosphate forms a precipitate in the reaction mixture. The ***illumipro-10*** detects the change in light transmission through the reaction mixture created by the precipitating magnesium pyrophosphate. Sample results are reported as Positive or Negative based on the detected change in light transmission.

The ***illumigene*** Group B *Streptococcus* (GBS) External Control Kit consists of a Positive Control Reagent and a Negative Control Reagent. External Control reagents are provided to aid the user in detection of reagent deterioration, adverse environmental or test conditions, or variance in operator performance that may lead to test errors. The ***illumigene*** Group B *Streptococcus* External Control Kit is required for routine Quality Control.

J. Substantial Equivalence Information:

1. Predicate device name(s):
   illumigene Group B *Streptococcus* (GBS) Assay
2. Predicate 510(k) numbers:
   K112125
3. Comparison with predicates:

Similarities		
Item	**DEVICE** ***illumigene*® GBS** **K121044**	**PREDICATE** ***illumigene*® GBS** **K112125**
Intended Use	Qualitative	Same
Test Principle	DNA Amplification Assay	Same
DNA Amplification Technology	Loop-Mediated Isothermal Amplification (LAMP)	Same
Target Sequences Detected	213 base pair (bp) sequence residing in the 593-805 bp region of *S. agalactiae* genome Segment 3	Same
Specimen Types	• Vaginal/Rectal Swab Specimen Enriched in Lim Broth • Vaginal/Rectal Swab Specimen Enriched in TransVag Broth	Same
Reagents/Components	• ***illumigene*** Control Reagent • ***illumigene*** Reaction Buffer • ***illumigene*** GBS Test Device • ***illumigene*** Heat Treatment Tubes	Same
Amplification	Self contained and automated	Same
Detection	Self contained and automated	Same
Testing Time	60 minutes	Same
Instrumentation	***illumipro-10™*** Automated Isothermal Amplification and Detection System	Same
Reading Method	Visible Light Transmission	Same
Calibration	Not required	Same

Differences		
Item	**DEVICE** *illumigene*® **GBS** **K121044**	**PREDICATE** *illumigene*® **GBS** **K112125**
Specimen Types	Vaginal/Rectal Swab Specimen Enriched in Carrot Broth	N/A
Performance		
• **Sensitivity**	**98.6%** [95% CI: 96.5% - 99.5%]	**97.4%** [95% CI: 91.9% - 99.0%]
• **Specificity**	**93.2%** [95% CI: 91.6% - 94.5%]	**92.3%** [95% CI: 90.0% - 94.1%]

K. Standard/Guidance Document Referenced (if applicable):

- Clinical and Laboratory Standards Institute. 2008. User Protocol for Evaluation of Qualitative Test Performance; Approved Guideline- Second Edition (EP12-A)
- Clinical and Laboratory Standards Institute. 2005. User Verification of Performance for Precision and Trueness; Approved Guideline- Second Edition (EP15-A2)
- Clinical and Laboratory Standards Institute. 2005. Interference Testing in Clinical Chemistry; Approved Guideline- Second Edition (EP7-A2)

L. Test Principle:

The ***illumigene*** Group B *Streptococcus* assay is based on loop-mediated isothermal amplification technology (LAMP). Loop-mediated amplification of DNA is accomplished by the use of specially designed primers that provide specific and continuous isothermal amplification. Magnesium-pyrophosphate is produced as a by-product of LAMP amplification. The magnesium-pyrophosphate forms a white precipitate in the reaction solution, giving the reaction solution a turbid appearance. Change in sample absorbance created by precipitation of magnesium pyrophosphate indicates the presence of target DNA and is considered a positive reaction. The absence of target DNA results in no detectable change in sample absorbance and is considered a negative reaction.

M. Performance Characteristics (if/when applicable):

1. Analytical Performance:

a. Precision/Reproducibility:

Reproducibility studies were completed with K112125. Blind coded panels of 10 samples were supplied to three independent laboratories. Samples were randomly sorted within each panel to mask sample identities. The panels included contrived samples manufactured as low positive samples (i.e. limit of detection, n = 3) and high negative samples (n = 3). The panels also included contrived positive (n = 3) samples and natural negative samples (n = 1). Testing was performed by different operators at each site on the same day (intra-assay variability) for five days (inter-assay variability). Three lots of ***illumigene*** GBS and five ***illumipro-10*** instruments were used in this study. The results are given in the table below:

	Site 1		Site 2		Site 4		Total	
Sample Type	**Percent agreement**		**Percent agreement**		**Percent agreement**		**Percent agreement**	
Negative	10/10	100%	10/10	100%	10/10	100%	30/30	100%
High Negative	30/30	100%	30/30	100%	30/30	100%	90/90	100%
Low Positive	30/30	100%	30/30	100%	30/30	100%	90/90	100%
Positive	30/30	100%	30/30	100%	30/30	100%	90/90	100%

b. *Linearity/assay reportable range:*

Not applicable as this assay is qualitative

c. *Traceability, Stability, Expected values (controls, calibrators, or methods):*

Stability:
Stability studies were completed with K112125 and supplemented for K121044. Sample storage and hold time studies were performed to characterize ***illumigene***® Group B *Streptococcus* (GBS) assay ranges. Validation studies performed at Meridian indicated that Lim Broth represented the worst-case matrix; therefore studies were completed using Lim Broth. Assay ranges were confirmed for the remaining TransVag Broth and Carrot Broth by testing one high negative and one LoD positive sample prepared from each broth.

Study results demonstrated that undiluted samples can be held at 19 -27 C for up to 6 hours or at 2-8 C for up to 7 days after culture enrichment and prior to testing. Samples diluted with ***illumigene***® Control Reagent can be held at 21 -27 C for up to 15 minutes prior to heat-treatment. Heat-treated samples may be held at 19-29 C for up to 45 minutes prior to further processing.

Sample freeze/thaw studies were also performed. Samples were enriched 18-24 hours and frozen prior to initiation of testing. Samples were subject to multiple freeze/thaw cycles. Study results showed that samples should *not* be freeze/thawed.

Final testing demonstrated that Lim Broth, in combination with Dacron/polyester, flocked nylon and foam swab types perform acceptably with the ***illumigene***® GBS assay. Amies Clear and Calcium Alginate Swabs produced invalid results and are not considered validated for use with ***illumigene***® GBS. Swab types with demonstrated performance in the ***illumigene***® GBS assay appear in the Package Insert.

d. *Detection limit:*

Detection limit studies were completed with K112125. Sensitivity studies were designed to determine the analytical limit of detection of S. agalactiae in Lim Broth. Six common strains of S.agalactiae, representing six serotypes, were evaluated with the ***illumigene***® GBS assay. Each strain was spiked into negative Lim Broth and diluted serially. A minimum of twenty replicates for each dilution were individually processed and tested to establish LoD. Testing was performed using three production lots of ***illumigene***® GBS assay and six ***illumipro-10***™ instruments. External Positive and Negative Controls were tested each day throughout the study.

The LoD of the assay ranged from 60 CFU/Test to 1280 CFU/Test. The table below shows the lowest concentration for each serotype that produced positive results for 95% of the replicates tested.

Serotype	*Streptococcus agalactiae* Strain Description	CFU/Test
Ia	NCTC 11248	60
Ib	ATCC 12401	80
Ic	NCTC 11253	640
II	II/2	320
III	ATCC 12403	160
V	ATCC BAA-611	1280

Additional *S. agalactiae* strains were tested and produced positive reactions at 1280 CFU/test with ***illumigene*** GBS. Strains and serotypes were tested as follows: **Serotype IV**: NCTC 11930, hemolytic; **Serotype VIa:** NCTC 08188, non-hemolytic; Serotype **VII:** VII/2, hemolytic; **Serotype VIII:** VIII/2, hemolytic; **Serotype X**: NCTC 11249, hemolytic; **Unknown Serotype:** ATCC 13813, non-hemolytic; and ATCC12386, hemolytic.

Limit of Detection studies are acceptable.

e. *Analytical specificity:*

Interference Testing:

Interference testing was completed with K112125. Selected substances that might be expected to be present in vaginal/rectal swab samples taken from antepartum women were added to a negative Lim broth sample and two contrived positive Lim broth samples. The negative sample was prepared by pooling confirmed negative Lim Broth samples while the contrived positive samples were prepared by spiking a pooled, confirmed negative Lim sample with either *Streptococcus agalactiae*, strain 11248 Serotype Ia (123 CFU/test) or *Streptococcus agalactiae*, strain 12401 Serotype Ib (80 CFU/test). Potentially interfering substances were added to Lim broth samples at final concentrations of 2.5% v/v or greater when the substances could be pipetted. Substances that could not be pipetted were coated onto cotton swabs, immersed in the negative/positive Lim broth samples and tested. Dilution Controls were prepared by adding a phosphate buffered saline solution in place of the potentially cross-reactive organisms. Each inoculated sample was tested in triplicate.

The following substances, at the specified saturated solvent/diluents concentrations, do not interfere with ***illumigene*** Group B *Streptococcus* test results: Amniotic fluid (10% v/v), Human DNA (100 ng/Test), Urine (30%v/v), Whole Blood (2.5% v/v). The following substances do not interfere with test results: Meconium, Stool, Hemorrhoidal cream (30.65 mg/100mg), Miconazole (fungicide), Mucin (0.5-1.5%), Spermicidal gel (nonoxynol 9) (4 mg/100mg). Lubricating gel produced False Negative Results in 1 of 11 replicates tested. Body Powder produced False Negative Results in 1 of 10 replicates tested. Whole Blood at concentrations greater than 2.5% v/v interferes with the ***illumigene*** GBS assay.

Interference studies are acceptable.

Cross-Reactivity Study:

Cross-reactivity studies were completed with K112125. Potentially cross-reacting microorganisms expected to be present in vaginal/rectal swab specimens were added to negative and contrived positive Lim Broth samples. The negative sample was prepared by pooling confirmed negative Lim Broth samples. The contrived positive sample was prepared by spiking a confirmed negative matrix with *Streptococcus*

agalactiae, strain 12401, at 122 CFU/test, near the limit of detection for this strain. Potentially cross-reactive microorganisms were added at concentrations of 1.2×10^8 CFU/mL (bacteria and fungi) or virus at a minimum of 1×10^5 $TCID_{50}$/mL (viruses). Dilution controls for each sample were prepared by adding sterile saline solution in place of the potentially cross-reactive microorganisms. Each sample was tested in triplicate. Cross-reactivity with *Enterococcus dispar* was observed in one of seven replicates tested.

The following microorganisms at the indicated concentrations do not interfere with ***illumigene*** GBS: *Aeromonas hydrophila, Alcaligenes faecalis, Bacillus cereus, Bacillus subtilis, Bacteroides fragilis, Campylobacter coli, Campylobacter fetus, Campylobacter jejuni, Candida albicans, Candida glabrata, Candida krusei, Candida parapsilosis, Candida tropicalis, Citrobacter freundii, Clostridium bifermentans, Clostridium butyricum, Clostridium difficile, Clostridium histolyticum, Clostridium novyi, Clostridium perfringens, Clostridium septicum, Clostridium sordellii, Clostridium sporogenes, Clostridium tetani, Corynebacterium genitalium, Corynebacterium urealyticum, Corynebacterium xerosis, Enterobacter aerogenes, Enterobacter cloacae, Enterococcus avium, Enterococcus durans, Enterococcus faecalis, Enterococcus faecium, Escherichia coli, Escherichia coli 0157:H7, Escherichia fergusonii, Escherichia hermannii, Gardnerella vaginalis, Haemophilus ducreyi, Helicobacter pylori, Klebsiella pneumoniae, Lactobacillus acidophilus, Lactobacillus brevis, Lactobacillus casei, Lactobacillus delbruekii subspecies lactis, Lactobacillus jensenii, Lactococcus lactis, Legionella pneumophila, Listeria monocytogenes, Moraxella osloensis, Morganella morganii, Neisseria gonorrhoeae, Peptostreptococcus anaerobius, Plesiomonas shigelloides, Porphyromonas asaccharolytica, Prevotella melaninogenica, Propionibacterium acnes, Proteus mirabilis, Proteus vulgaris, Pseudomonas aeruginosa, Pseudomonus fluorescens, Salmonella Group B, Salmonella Group C, Salmonella Group D, Salmonella Group E, Serratia liquefaciens, Serratia marcescens, Shigella boydii, Shigella flexneri, Shigella sonnei, Staphylococcus aureus, Staphylococcus aureus (Cowan), Staphylococcus epidermidis, Staphylococcus saprophyticus, Streptococcus anginosus, Streptococcus bovis, Streptococcus dysgalactiae equisimilis, Streptococcus intermedius, Streptococcus mitis, Streptococcus oralis, Streptococcus pneumoniae, Streptococcus pyogenes, Streptococcus salivarius, Streptococcus sanguinis, Vibrio parahaemolyticus, Yersinia enterocolitica,* Adenovirus 40, Adenovirus 41, BK virus, Coxsackievirus, Echovirus, Epstein Barr virus, Herpes Simplex Virus-1, Herpes Simplex Virus-2, Rotavirus.

Mycoplasma genitalium, Mycoplasma hominis and Ureaplasma urealyticum were tested at final concentrations ranging between 1.6×10^6 and 9.9×10^6 CFU/mL with no reaction with the ***illumigene*** GBS assay.

Cross-reactivity studies are acceptable.

f. Assay cut-off:

The ***illumigene*** Group B *Streptococcus* Assay has a fixed cut-off based on the measured change in light transmission at the assay endpoint. The ***illumipro-10*** measures transmission of light through the Test and the Control reactions at the start of the Assay Run ($Signal_{initial}$) and at the end of the Assay Run ($Signal_{final}$). The ***illumipro-10*** calculates that change in transmission between the $Signal_{final}$: $Signal_{initial}$ and compares the result to a fixed cut-off value. Test results are reported as Positive or Negative based on comparison to the assay cut-off. Fixed cut-off values were based on well characterized clinical specimens.

2. Comparison Studies:
   a. *Method comparison with predicate device:*

      Not applicable

   b. *Matrix comparison:*

      Not applicable

3. Clinical Studies:

   a. *Clinical Sensitivity:*
   Clinical trials for the ***illumigene*** Group B *Streptococcus* (GBS) assay, including the ***illumipro-10*** Automated Isothermal amplification and detection system, were conducted in 2011 and 2012. Performance characteristics of the ***illumigene*** GBS assay were determined by comparison to GBS bacterial culture in two separate studies: (1) Lim and TransVag Broth Enrichment, reference K112125; and (2) Carrot Broth Enrichment. Combined performance data for all studies and all enrichment broth types is shown in Table 1.

***Table 1: illumigene* Group B *Streptococcus* assay performance characteristics**

Sample Type	Positive Samples			Negative Samples		
	illumigene / GBS Culture	Sensitivity %	95% CI	*illumigene* / GBS Culture	Specificity %	95% CI
Total	**285/289**	**98.6%**	**96.5 – 99.5%**	**1045/1121**	**93.2%**	**91.6 – 94.5%**
Lim Broth	82/84	97.6%	91.7 – 99.3%	296/315	94.0%	90.8 – 96.1%
TransVag Broth	68/70	97.1%	90.2 – 99.2%	314/346	90.8%	87.2 – 93.4%
Carrot Broth	135/135	100%	97.2 – 100.0%	435/460	94.6%	92.1 – 96.3%

(1) Lim and TransVag Broth Enrichment: ***illumigene*** GBS assay performance using Lim Broth and TransVag Broth enriched specimens was evaluated in 2011 by four independent clinical test sites located in the Midwestern and Southern regions of the United States. A total of 826 qualified patient samples were evaluated. Samples were obtained according to established guidelines for the collection of clinical specimens for culture of Group B *Streptococcus* and enriched for 18-24 hours in either Lim Broth or TransVag Broth prior to ***illumigene*** testing. Four hundred three (403, 48.8%) specimens were enriched with Lim Broth and 423 (51.2%) specimens were enriched with TransVag Broth prior to testing. The age groups of patients tested ranged from 15 years of age to 44 years of age, with age unknown for 3 (0.4%) of the patient population. No differences in test performance were observed based on enrichment medium or patient age. Overall assay Sensitivity was reported as 97.4% [95% CI: 91.9% - 99.0%] where Specificity was 92.3% [95% CI: 90.0% - 94.1%]. Table 2 shows assay shows overall assay performance reported for the study; Table 3 summarizes assay performance by Clinical Site.

Table 2. Lim and TransVag enrichment performance data

Group B *Streptococcus* Culture	*illumigene* Group B *Streptococcus* (GBS)		
	Positive	**Negative**	**Total**
Positive	150	4	154
Negative	51	610	661
Total	201	614	815
			95% CI
Sensitivity	150/154	97.4%	91.9 – 99.0%
Specificity	610/661	92.3%	90.0 – 94.1%
Correlation	760/815	93.3%	91.3 – 94.8%

Forty-eight of the 51 false positive results were positive by another molecular method. Invalid results were obtained for 11/826 samples tested or 1.3%. Two of the 11 samples remained invalid after repeat testing of the original sample.

Table 3: Performance characteristics summary; Lim and TransVag Broth Enrichment

Site Identification	**Enrichment Broth**	**Positive Samples**			**Negative Samples**		
		***illumigene* /GBS Culture**	**% Sensitivity**	**95% CI**	***illumigene* /GBS Culture**	**% Specificity**	**95% CI**
Total	**N/A**	**150/154**	**97.4%**	**91.9 – 99.0%**	**610/661**	**92.3%**	**90.0 – 94.1%**
Site 1	TransVag	32/33	97.0%	84.7 – 99.5%	197/199	99.0%	96.4 – 99.7%
Site 3	TransVag	36/37	97.3%	86.2 - 99.5%	117/147	79.6%	72.4 - 85.3%
Site 2	Lim	38/39	97.4%	86.8 - 99.5%	162/168	96.4%	92.4 – 98.4%
Site 4	Lim	44/45	97.8%	88.4 – 99.6%	134/147	97.8%	85.5 – 94.8%

Specimens that generated discrepant results were further evaluated by independent testing laboratories using FDA cleared or laboratory validated molecular assays. Sixteen of nineteen Lim Broth False Positive results were positive by an alternate molecular method. All thirty-two TransVag Broth False Positive results were positive by an alternate molecular method. In addition to discrepant sample analysis, a selection of concordant samples was tested with non-***illumigene*** molecular methodologies. Concordant result testing showed a combined correlation between molecular methods of 97.7%.

(2) Carrot Broth Enrichment: Performance characteristics specific to Carrot Broth Enrichment were established by studies involving three independent clinical test sites located in the Midwestern and Southern regions of the United States. Independent clinical test sites located in the Midwestern and Southern regions of the United States evaluated a total of 600 qualified patient samples. Samples were obtained according to established guidelines for the collection of clinical specimens for culture of Group B *Streptococcus* and enriched in Carrot Broth prior to ***illumigene*** testing. The age groups of patients tested ranged from 15 years of age to 48 years of age; no differences in test performance were observed based on patient age. Table 4 shows assay performance reported for the study; Table 5 summarizes assay performance by Clinical Site.

***Table 4: illumigene* Group B *Streptococcus* assay performance; Carrot Broth Enrichment**

Group B *Streptococcus* Culture	*illumigene* Group B *Streptococcus (GBS)*		
	Positive	Negative	Total
Positive	135	0	135
Negative	25	435	460
Total	160	435	595
			95% CI
Sensitivity	135/135	100.0%	97.2 - 100.0%
Specificity	435/460	94.6%	92.1 - 96.3%
Correlation	570/595	95.8%	93.9 - 97.1%

Invalid results were obtained for 5/600 (0.8%) samples. One of the 5 samples remained invalid after repeat testing. Repeat test results are not included in assay performance calculations. Twenty four of the 25 ***illumigene*** Positive: GBS Culture Negative specimens were further analyzed by an independent laboratory developed GBS Molecular Assay. Sixteen of the 24 discrepant samples were positive by the alternate molecular amplification assay.

***Table 5: illumigene* Group B *Streptococcus* assay performance by Site**

Site Identification	Positive Samples			Negative Samples			Invalid Samples	
	illumigene / GBS Culture	% Sensitivity	95% CI	*illumigene* /GBS Culture	% Specificity	95% CI	Invalid /Total	% Invalid
Total	135/135	100.0%	97.2 - 100.0%	435/460	94.6%	92.1 - 96.3%	5/600	0.8%
Site 1	58/58	100.0%	93.8 - 100.0%	92/93	98.9%	94.2 - 99.8%	0/151	0.0%
Site 2	36/36	100.0%	90.4 - 100.0%	145/149	97.3%	93.3 - 99.0%	1/186	0.5%
Site 3	41/41	100.0%	91.4 - 100.0%	198/218	90.8%	86.3 - 94.0%	4/263	1.5%

Enriched carrot broth samples were visually inspected for color at the end of the enrichment incubation and prior to initiation of ***illumigene*** testing. Table 3 summarizes performance data and observed broth color. Thirty four of the 135 (25.1%) ***illumigene***/GBS Culture positive specimens were reported as showing no visual change in color at the end of enrichment incubation.

***Table 6:* Performance Characteristics by Carrot Broth Results**

Sample Type	Positive Samples			Negative Samples		
	illumigene / GBS Culture	Sensitivity %	95% CI	*illumigene* / GBS Culture	Specificity %	95% CI
Color Change	100/100	100.0%	96.3 - 100.0%	2/2	100.0%	34.2 - 100.0%
No Color Change	34/34	100.0%	89.8 - 100.0%	433/458	94.5%	92.1 - 96.3%
Unspecified	1/1	100.0%	20.7 - 100.0%	0/0	0.0	0.0 - 0.0%

b. Clinical Specificity:

See Section 3a

c. Other Clinical Supportive Data

Not applicable

4. Clinical cut-off:

Not applicable

5. Expected values/Reference range:

Approximately 10-30% of antepartum women are colonized with Group B *Streptococcus* in the vagina or rectum. Clinical performance of the ***illumigene*** GBS Assay was established during two clinical studies completed in 2011 (Lim Broth and TransVag Broth) and 2012 (Carrot Broth). The overall incidence of GBS colonization in antepartum women tested during the 2011 study was 24.3% (201 of 826). Incidence of GBS colonization for enrichment performed using Lim Broth was found to be 25.1% (101 of 403); while incidence for specimens enriched by TransVag Broth was found to be 23.6% (100 of 423). The overall incidence of GBS colonization in antepartum women tested during the 2012 Carrot Broth study was found to be 22.5% (135 of 600).

N. Other Supportive Device and Instrument Information:

Instrument: ***illumipro-10™***

O. System Descriptions:

System Description was reviewed in previous submission, K100818, K110012 and K112125. No system or software changes were made.

1. Modes of Operation:

The ***illumipro-10™*** heats each ***illumigene***® GBS Test Device containing prepared samples and Control Reagent, facilitating amplification of target DNA. When *S. agalactiae* is present in the enriched culture sample, a conserved sequence of the *S. agalactiae* is amplified and magnesium pyrophosphate is formed. Magnesium pyrophosphate forms a precipitate in the reaction mixture. The ***illumipro-10*** detects the change in light transmission through the reaction mixture created by the precipitating magnesium pyrophosphate. Sample results are reported as Positive or Negative based on the detected change in light transmission.

2. Software:

FDA has reviewed applicant's Hazard Analysis and software development processes for this line of product types:

Yes_____X_____ No_____

3. Specimen Identification:

The ***illumipro-10™*** utilizes software to automate incubation and detection of ***illumigene*** Molecular Diagnostic in vitro diagnostic test reactions. The ***illumipro-10™*** reports sample results as INVALID, POSITIVE or NEGATIVE.

4. Specimen Sampling and Handling:

   Specimens are prepared manually. Incubation and detection are automated using the ***illumipro-10™***.

5. Calibration:

   Calibration of the ***illumipro-10™*** is not required.

6. Quality Control:

   The ***illumigene***® Group B Streptococcus External Control Kit consists of a Positive Control Reagent and a Negative Control Reagent. External Control reagents are provided to aid the user in detection of reagent deterioration, adverse environmental or test conditions, or variance in operator performance that may lead to test errors. The ***illumigene***® Group B Streptococcus External Control Kit is required for routine Quality Control.

Statement for the Record, K 121044
Meridian BioScience, Inc.
Illumigene Group B Streptococcus (GBS) DNA Amplification Assay

This 510(k) was reviewed under OIVD's Pilot Triage Program. This program represents an internal workload management tool intended to reduce internal FDA review resources for 510(k) applications that are of good quality upon receipt by FDA.

The information in the 510(k) is complete and supports a substantial equivalence (SE) determination. Please refer to the applicant's 510(k) summary for a summary of the information that supports this SE determination.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration

10903 New Hampshire Avenue
Silver Spring, MD 20993

Meridian Bioscience, Inc.
C/o Michelle L. Smith
Senior Director, RA/DA
3471 River Hills Drive
Cincinnati, Ohio 45244

MAY - 1 2012

Re: k121044
Trade/Device Name: ***illumigene***® Group B Streptococcus (GBS) DNA Amplification Assay
Regulation Number: 21 CFR 888.3740
Regulation Name: Streptococcus spp. serological reagents
Regulatory Class: Class I
Product Code: NJR
Dated: April 5, 2012
Received: April 6, 2012

Dear Ms. Smith:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part 801); medical device reporting (reporting of medical

device-related adverse events) (21 CFR 803); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801), please go to http://www.fda.gov/AboutFDA/CentersOffices/CDRH/CDRHOffices/ucm115809.htm for the Center for Devices and Radiological Health's (CDRH's) Office of Compliance. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm for the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

You may obtain other general information on your responsibilities under the Act from the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm.

Sincerely yours,

Sally A. Hojvat, M.Sc., Ph.D.
Director
Division of Microbiology Devices
Office of *In Vitro* Diagnostics Device
Evaluation and Safety
Office of Device Evaluation
Center for Devices and
Radiological Health

Enclosure

Indication(s) for Use Form

510(k) Number: K121044

Device Name: ***illumigene*** Group B *Streptococcus* (GBS) DNA Amplification Assay

Indications for Use:

The ***illumigene*** Group B *Streptococcus* (GBS) assay, performed on the ***illumipro-10™***, is a qualitative in vitro diagnostic for the detection of *Streptococcus agalactiae* in enriched cultures obtained from vaginal/rectal swab specimens from antepartum women. Enriched cultures are obtained by 18-24 hour incubation of vaginal/rectal swab specimens in selective broth medium, either Lim Broth, TransVag Broth or Carrot Broth.

The ***illumigene*** GBS assay utilizes loop-mediated isothermal DNA amplification (LAMP) technology to detect *Streptococcus agalactiae* by targeting a segment of the *Streptococcus agalactiae* genome. Results from the ***illumigene*** GBS assay can be used as an aid in establishing the GBS colonization status of antepartum women. This assay is not intended to diagnose or monitor treatment for GBS infections.

The ***illumigene*** GBS assay does not provide susceptibility results. Culture isolates are needed for performing susceptibility testing as recommended for penicillin-allergic women.

illumigene Group B *Streptococcus* is intended for use in hospital, reference or state laboratory settings. The device is not intended for point-of-care use.

Prescription Use ___X____ Over-The-Counter Use _____

(Part 21 CFR 801 Subpart D) AND/OR (21 CFR 801 Subpart C)

(PLEASE DO NOT WRITE BELOW THIS LINE-CONTINUE ON ANOTHER PAGE OF NEEDED)

Concurrence of CDRH, Office of In Vitro Diagnostic Devices (OIVD)

Division Sign-Off
Office of In Vitro Diagnostic Device
Evaluation and Safety

510(k) K~~1~~044 (Sol)

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